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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/620,586	07/20/2000	Steen Klysner	0459-0464P	2471

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EXAMINER

JAMROZ, MARGARET E

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 02/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/620,586

Applicant(s)

KLYSNER ET AL.

Examiner

Margaret E Jamroz

Art Unit

1644

-- Th MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 July 2000.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-52 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-52 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: See Continuation Sheet.

Continuation of Attachment(s) 6). Other: (1) restriction election facsimile and (2) Notice to comply with the Sequence Rules

Notice to Comply

Application No.

09/620,586

Examiner

Margaret E Jamroz

Applicant(s)

KLYSNER ET AL.

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NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- ☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☐ 7. Other:

Applicant Must Provide:

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

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PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY

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DETAILED ACTION

1. The location of your application in the PTO has changed. To aid in correlating papers for this application, all further correspondence regarding this application should be directed to Megan Jamroz in Art Unit 1644, Technology Center 1600.

Sequence Compliance

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant is reminded to amend the entire specification (including the Brief Description of Drawings) and claims as appropriate to reflect compliance with the Sequence Rules. For example, the specification on page 25, line 26 contains an amino acid sequence that is not in compliance with the Sequence Rules.

Restriction Requirement

3. Please Note: In an effort to enhance communication with our customers and reduce processing time, Group 1640 is running a Fax Response Pilot for Written Restriction Requirements. A dedicated Fax machine is in place to receive your responses. The Fax number is 703-308-4315. A Fax cover sheet is attached to this Office Action for your convenience. We encourage your participation in this Pilot program. If you have any questions or suggestions please contact Paula Hutzell, Ph.D., Supervisory Patent Examiner at Paula.Hutzell@uspto.gov or 703-308-4310. Thank you in advance for allowing us to enhance our customer service. Please limit the use of this dedicated Fax number to responses to Written Restrictions.

In view of the delays in the mail at the present time, the office strongly encourages faxing responses.

4. Restriction to one of the following inventions is required under 35 U.S.C. § 121:

1. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **OR** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

2. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **OR** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (**B**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

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3. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **OR** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one second moiety that stimulates the immune system (**C**) is introduced

4. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **OR** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

5. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **OR** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**) and at least one first moiety that effects targeting (**B**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

6. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **OR** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**) and at least one second moiety that stimulates the immune system (**C**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

7. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **OR** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**) and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

8. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **OR** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (**B**) and at least one second moiety that stimulates the immune system (**C**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

9. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **OR** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (**B**) and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

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10. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **OR** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one second moiety that stimulates the immune system (**C**) and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

11. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **OR** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**), at least one first moiety that effects targeting (**B**), and at least one second moiety that stimulates the immune system (**C**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

12. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **OR** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**), at least one first moiety that effects targeting (**B**), and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

13. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **OR** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**), at least one second moiety that stimulates the immune system (**C**), and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

14. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **OR** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (**B**), at least one second moiety that stimulates the immune system (**C**), and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

15. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **OR** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**), at least one first moiety that effects targeting (**B**), at least one second moiety that stimulates the immune system (**C**), and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

16. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **AND** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign T helper epitope moiety (**A**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

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17. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **AND** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (**B**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.
18. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **AND** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one second moiety that stimulates the immune system (**C**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.
19. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **AND** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.
20. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **AND** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**) and at least one first moiety that effects targeting (**B**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.
21. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **AND** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**) and at least one second moiety that stimulates the immune system (**C**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.
22. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **AND** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**) and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.
23. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **AND** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (**B**) and at least one second moiety that stimulates the immune system (**C**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.
24. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **AND** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (**B**) and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

25. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **AND** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one second moiety that stimulates the immune system (**C**) and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

26. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **AND** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**), at least one first moiety that effects targeting (**B**), and at least one second moiety that stimulates the immune system (**C**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

27. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **AND** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**), at least one first moiety that effects targeting (**B**), and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

28. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **AND** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**), at least one second moiety that stimulates the immune system (**C**), and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

29. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **AND** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (**B**), at least one second moiety that stimulates the immune system (**C**), and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

30. Claims 1-23 and 29, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof **AND** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**), at least one first moiety that effects targeting (**B**), at least one second moiety that stimulates the immune system (**C**), and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 424, subclasses 184.1, 185.1, and 195.11.

31. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **OR** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**) is introduced; classified in Class 514, subclass 44.

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32. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **OR** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (**B**) is introduced; classified in Class 514, subclass 44.

33. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **OR** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one second moiety that stimulates the immune system (**C**) is introduced; classified in Class 514, subclass 44.

34. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **OR** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 514, subclass 44.

35. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **OR** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**) and at least one first moiety that effects targeting (**B**) is introduced; classified in Class 514, subclass 44.

36. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **OR** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**) and at least one second moiety that stimulates the immune system (**C**) is introduced; classified in Class 514, subclass 44.

37. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **OR** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**) and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 514, subclass 44.

38. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **OR** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (**B**) and at least one second moiety that stimulates the immune system (**C**) is introduced; classified in Class 514, subclass 44.

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39. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **OR** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (**B**) and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 514, subclass 44.

40. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **OR** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one second moiety that stimulates the immune system (**C**) and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 514, subclass 44.

41. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **OR** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**), at least one first moiety that effects targeting (**B**), and at least one second moiety that stimulates the immune system (**C**) is introduced; classified in Class 514, subclass 44.

42. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **OR** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**), at least one first moiety that effects targeting (**B**), and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 514, subclass 44.

43. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **OR** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**), at least one second moiety that stimulates the immune system (**C**), and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 514, subclass 44.

44. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **OR** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (**B**), at least one second moiety that stimulates the immune system (**C**), and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 514, subclass 44.

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45. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **OR** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (A), at least one first moiety that effects targeting (B), at least one second moiety that stimulates the immune system (C), and at least one third moiety that optimizes presentation (D) is introduced; classified in Class 514, subclass 44.

46. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **AND** at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign T helper epitope moiety (A) is introduced; classified in Class 514, subclass 44.

47. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **AND** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (B) is introduced; classified in Class 514, subclass 44.

48. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **AND** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one second moiety that stimulates the immune system (C) is introduced; classified in Class 514, subclass 44.

49. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **AND** a nucleic acid encoding at least one GDF-8 analogue wherein the analogue has been modified so that at least one third moiety that optimizes presentation (D) is introduced; classified in Class 514, subclass 44.

50. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **AND** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (A) and at least one first moiety that effects targeting (B) is introduced; classified in Class 514, subclass 44.

51. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **AND** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (A) and at least one second moiety that stimulates the immune system (C) is introduced; classified in Class 514, subclass 44.

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52. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **AND** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**) and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 514, subclass 44.

53. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **AND** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (**B**) and at least one second moiety that stimulates the immune system (**C**) is introduced; classified in Class 514, subclass 44.

54. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **AND** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (**B**) and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 514, subclass 44.

55. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **AND** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one second moiety that stimulates the immune system (**C**) and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 514, subclass 44.

56. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **AND** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**), at least one first moiety that effects targeting (**B**), and at least one second moiety that stimulates the immune system (**C**) is introduced; classified in Class 514, subclass 44.

57. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **AND** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**), at least one first moiety that effects targeting (**B**), and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 514, subclass 44.

58. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **AND** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**), at least one second moiety that stimulates the immune system (**C**), and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 514, subclass 44.

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59. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **AND** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (**B**), at least one second moiety that stimulates the immune system (**C**), and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 514, subclass 44.

60. Claims 24-28 and 43-45, drawn to a method for *in vivo* down-regulation of GDF-8 comprising administering a nucleic acid encoding at least one GDF-8 polypeptide, or fragment thereof **AND** a nucleic acid encoding at least one GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**), at least one first moiety that effects targeting (**B**), at least one second moiety that stimulates the immune system (**C**), and at least one third moiety that optimizes presentation (**D**) is introduced; classified in Class 514, subclass 44.

61. Claims 30 and 32-33, drawn to a GDF-8 analog, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**) is introduced, and compositions thereof; classified in Class 530, subclass 350, and Class 424, subclasses 185.1, and 195.11, respectively.

62. Claims 30 and 32-33, drawn to a GDF-8 analog, wherein the analogue has been modified so that at least one GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (**B**) is introduced, and compositions thereof; classified in Class 530, subclass 350, and Class 424, subclasses 185.1, and 195.11, respectively.

63. Claims 30 and 32-33, drawn to a GDF-8 analog, wherein the analogue has been modified so that at least one second moiety that stimulates the immune system (**C**) is introduced, and compositions thereof; classified in Class 530, subclass 350, and Class 424, subclasses 185.1, and 195.11, respectively.

64. Claims 30 and 32-33, drawn to a GDF-8 analog, wherein the analogue has been modified so that at least one third moiety that optimizes presentation (**D**) is introduced, and compositions thereof; classified in Class 530, subclass 350, and Class 424, subclasses 185.1, and 195.11, respectively.

65. Claims 30 and 32-33, drawn to a GDF-8 analog, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**) and at least one first moiety that effects targeting (**B**) is introduced, and compositions thereof; classified in Class 530, subclass 350, and Class 424, subclasses 185.1, and 195.11, respectively.

66. Claims 30 and 32-33, drawn to a GDF-8 analog, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**) and at least one second moiety that stimulates the immune system (**C**) is introduced, and compositions thereof; classified in Class 530, subclass 350, and Class 424, subclasses 185.1, and 195.11, respectively.

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67. Claims 30 and 32-33, drawn to a GDF-8 analog, wherein the analogue has been modified so that at least one foreign Th epitope moiety (A) and at least one third moiety that optimizes presentation (D) is introduced, and compositions thereof; classified in Class 530, subclass 350, and Class 424, subclasses 185.1, and 195.11, respectively.

68. Claims 30 and 32-33, drawn to a GDF-8 analog, wherein the analogue has been modified so that at least one first moiety that effects targeting (B) and at least one second moiety that stimulates the immune system (C) is introduced, and compositions thereof; classified in Class 530, subclass 350, and Class 424, subclasses 185.1, and 195.11, respectively.

69. Claims 30 and 32-33, drawn to a GDF-8 analog, wherein the analogue has been modified so that at least one one first moiety that effects targeting (B) and at least one third moiety that optimizes presentation (D) is introduced, and compositions thereof; classified in Class 530, subclass 350, and Class 424, subclasses 185.1, and 195.11, respectively.

70. Claims 30 and 32-33, drawn to a GDF-8 analog, wherein the analogue has been modified so that at least one one second moiety that stimulates the immune system (C) and at least one third moiety that optimizes presentation (D) is introduced, and compositions thereof; classified in Class 530, subclass 350, and Class 424, subclasses 185.1, and 195.11, respectively.

71. Claims 30 and 32-33, drawn to a GDF-8 analog, wherein the analogue has been modified so that at least one foreign Th epitope moiety (A), at least one first moiety that effects targeting (B), and at least one second moiety that stimulates the immune system (C) is introduced, and compositions thereof; classified in Class 530, subclass 350, and Class 424, subclasses 185.1, and 195.11, respectively.

72. Claims 30 and 32-33, drawn to a GDF-8 analog, wherein the analogue has been modified so that at least one foreign Th epitope moiety (A), at least one first moiety that effects targeting (B), and at least one third moiety that optimizes presentation (D) is introduced, and compositions thereof; classified in Class 530, subclass 350, and Class 424, subclasses 185.1, and 195.11, respectively.

73. Claims 30 and 32-33, drawn to a GDF-8 analog, wherein the analogue has been modified so that at least one foreign Th epitope moiety (A), at least one second moiety that stimulates the immune system (C), and at least one third moiety that optimizes presentation (D) is introduced, and compositions thereof; classified in Class 530, subclass 350, and Class 424, subclasses 185.1, and 195.11, respectively.

74. Claims 30 and 32-33, drawn to a GDF-8 analog, wherein the analogue has been modified so that at least one first moiety that effects targeting (B), at least one second moiety that stimulates the immune system (C), and at least one third moiety that optimizes presentation (D) is introduced, and compositions thereof; classified in Class 530, subclass 350, and Class 424, subclasses 185.1, and 195.11, respectively.

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75. Claims 30 and 32-33, drawn to a GDF-8 analog, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**), at least one first moiety that effects targeting (**B**), at least one second moiety that stimulates the immune system (**C**), and at least one third moiety that optimizes presentation (**D**) is introduced, and compositions thereof; classified in Class 530, subclass 350, and Class 424, subclasses 185.1, and 195.11, respectively.

76. Claims 31 and 33, drawn to an immunogenic composition comprising an unmodified GDF-8 polypeptide; classified in Class 424, subclass 184.1.

77. Claims 34-42, 46-49, and 51-52, drawn to a nucleic acid fragment, a vector, a transformed cell, a stable cell line, a method for making the cell which encodes a GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**) is introduced, and compositions thereof; classified in Class 536, subclass 23.1, and Class 435, subclasses 320.1, 252.31, 252.8, 253.1, 254.2, 471, 254.11, 419, 325, 348, 69.1, and Class 514, subclass 44, respectively.

78. Claims 34-42, 46-49, and 51-52, drawn to a nucleic acid fragment, a vector, a transformed cell, a stable cell line, a method for making the cell which encodes a GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (**B**) is introduced, and compositions thereof; classified in Class 536, subclass 23.1, and Class 435, subclasses 320.1, 252.31, 252.8, 253.1, 254.2, 471, 254.11, 419, 325, 348, 69.1, and Class 514, subclass 44, respectively.

79. Claims 34-42, 46-49, and 51-52, drawn to a nucleic acid fragment, a vector, a transformed cell, a stable cell line, a method for making the cell which encodes a GDF-8 analogue, wherein the analogue has been modified so that at least one second moiety that stimulates the immune system (**C**) is introduced, and compositions thereof; classified in Class 536, subclass 23.1, and Class 435, subclasses 320.1, 252.31, 252.8, 253.1, 254.2, 471, 254.11, 419, 325, 348, 69.1, and Class 514, subclass 44, respectively.

80. Claims 34-42, 46-49, and 51-52, drawn to a nucleic acid fragment, a vector, a transformed cell, a stable cell line, a method for making the cell which encodes a GDF-8 analogue, wherein the analogue has been modified so that at least one third moiety that optimizes presentation (**D**) is introduced, and compositions thereof; classified in Class 536, subclass 23.1, and Class 435, subclasses 320.1, 252.31, 252.8, 253.1, 254.2, 471, 254.11, 419, 325, 348, 69.1, and Class 514, subclass 44, respectively.

81. Claims 34-42, 46-49, and 51-52, drawn to a nucleic acid fragment, a vector, a transformed cell, a stable cell line, a method for making the cell which encodes a GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (**A**) and at least one first moiety that effects targeting (**B**) is introduced, and compositions thereof; classified in Class 536, subclass 23.1, and Class 435, subclasses 320.1, 252.31, 252.8, 253.1, 254.2, 471, 254.11, 419, 325, 348, 69.1, and Class 514, subclass 44, respectively.

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82. Claims 34-42, 46-49, and 51-52, drawn to a nucleic acid fragment, a vector, a transformed cell, a stable cell line, a method for making the cell which encodes a GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (A) and at least one second moiety that stimulates the immune system (C) is introduced, and compositions thereof; classified in Class 536, subclass 23.1, and Class 435, subclasses 320.1, 252.31, 252.8, 253.1, 254.2, 471, 254.11, 419, 325, 348, 69.1, and Class 514, subclass 44, respectively.

83. Claims 34-42, 46-49, and 51-52, drawn to a nucleic acid fragment, a vector, a transformed cell, a stable cell line, a method for making the cell which encodes a GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (A) and at least one third moiety that optimizes presentation (D) is introduced, and compositions thereof; classified in Class 536, subclass 23.1, and Class 435, subclasses 320.1, 252.31, 252.8, 253.1, 254.2, 471, 254.11, 419, 325, 348, 69.1, and Class 514, subclass 44, respectively.

84. Claims 34-42, 46-49, and 51-52, drawn to a nucleic acid fragment, a vector, a transformed cell, a stable cell line, a method for making the cell which encodes a GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (B) and at least one second moiety that stimulates the immune system (C) is introduced, and compositions thereof; classified in Class 536, subclass 23.1, and Class 435, subclasses 320.1, 252.31, 252.8, 253.1, 254.2, 471, 254.11, 419, 325, 348, 69.1, and Class 514, subclass 44, respectively.

85. Claims 34-42, 46-49, and 51-52, drawn to a nucleic acid fragment, a vector, a transformed cell, a stable cell line, a method for making the cell which encodes a GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (B) and at least one third moiety that optimizes presentation (D) is introduced, and compositions thereof; classified in Class 536, subclass 23.1, and Class 435, subclasses 320.1, 252.31, 252.8, 253.1, 254.2, 471, 254.11, 419, 325, 348, 69.1, and Class 514, subclass 44, respectively.

86. Claims 34-42, 46-49, and 51-52, drawn to a nucleic acid fragment, a vector, a transformed cell, a stable cell line, a method for making the cell which encodes a GDF-8 analogue, wherein the analogue has been modified so that at least one one second moiety that stimulates the immune system (C) and at least one third moiety that optimizes presentation (D) is introduced, and compositions thereof; classified in Class 536, subclass 23.1, and Class 435, subclasses 320.1, 252.31, 252.8, 253.1, 254.2, 471, 254.11, 419, 325, 348, 69.1, and Class 514, subclass 44, respectively.

87. Claims 34-42, 46-49, and 51-52, drawn to a nucleic acid fragment, a vector, a transformed cell, a stable cell line, a method for making the cell which encodes a GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (A), at least one first moiety that effects targeting (B), and at least one second moiety that stimulates the immune system (C) is introduced, and compositions thereof; classified in Class 536, subclass 23.1, and Class 435, subclasses 320.1, 252.31, 252.8, 253.1, 254.2, 471, 254.11, 419, 325, 348, 69.1, and Class 514, subclass 44, respectively.

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88. Claims 34-42, 46-49, and 51-52, drawn to a nucleic acid fragment, a vector, a transformed cell, a stable cell line, a method for making the cell which encodes a GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (A), at least one first moiety that effects targeting (B), and at least one third moiety that optimizes presentation (D) is introduced, and compositions thereof; classified in Class 536, subclass 23.1, and Class 435, subclasses 320.1, 252.31, 252.8, 253.1, 254.2, 471, 254.11, 419, 325, 348, 69.1, and Class 514, subclass 44, respectively.

89. Claims 34-42, 46-49, and 51-52, drawn to a nucleic acid fragment, a vector, a transformed cell, a stable cell line, a method for making the cell which encodes a GDF-8 analogue, wherein the analogue has been modified so that at least foreign Th epitope moiety (A), at least one second moiety that stimulates the immune system (C), and at least one third moiety that optimizes presentation (D) is introduced, and compositions thereof; classified in Class 536, subclass 23.1, and Class 435, subclasses 320.1, 252.31, 252.8, 253.1, 254.2, 471, 254.11, 419, 325, 348, 69.1, and Class 514, subclass 44, respectively.

90. Claims 34-42, 46-49, and 51-52, drawn to a nucleic acid fragment, a vector, a transformed cell, a stable cell line, a method for making the cell which encodes a GDF-8 analogue, wherein the analogue has been modified so that at least one first moiety that effects targeting (B), at least one second moiety that stimulates the immune system (C), and at least one third moiety that optimizes presentation (D) is introduced, and compositions thereof; classified in Class 536, subclass 23.1, and Class 435, subclasses 320.1, 252.31, 252.8, 253.1, 254.2, 471, 254.11, 419, 325, 348, 69.1, and Class 514, subclass 44, respectively.

91. Claims 34-42, 46-49, and 51-52, drawn to a nucleic acid fragment, a vector, a transformed cell, a stable cell line, a method for making the cell which encodes a GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (A), at least one first moiety that effects targeting (B), at least one second moiety that stimulates the immune system (C), and at least one third moiety that optimizes presentation (D) is introduced, and compositions thereof; classified in Class 536, subclass 23.1, and Class 435, subclasses 320.1, 252.31, 252.8, 253.1, 254.2, 471, 254.11, 419, 325, 348, 69.1, and Class 514, subclass 44, respectively.

92. Claim 50, drawn to identification of a GDF-8 analogue, the method comprising preparing a GDF-8 analogue by **peptide synthesis**, testing members for the ability to induce production of antibodies, isolating polypeptides which induce antibody production against unmodified GDF-8; classified in Class 435, subclass 7.1.

93. Claims 50 and 52, drawn to identification of a GDF-8 analogue, the method comprising preparing a GDF-8 analogue by **genetic engineering**, testing members for the ability to induce production of antibodies, isolating polypeptides which induce antibody production against unmodified GDF-8; classified in Class 435, subclass 7.1.

94. Claim 51, drawn to a method for the preparation of an immunogenic composition comprising at least one modified GDF-8 polypeptide by **peptide synthesis**; classified in Class 530, subclass 333.

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4. Groups 61-91 are different products. Polypeptides, the analogues as claims, and the nucleic acids as claimed differ with respect to their structures and physicochemical properties; therefore each product is patentably distinct.

5. Groups 1-60 and 92-94 are different methods. The inventions as grouped in Groups 1-60 and 92-94 are distinct, each from the other, because they represent different inventive endeavors as one does not suggest the other; therefore, each method is patentably distinct.

The claims as written encompass a wide variety of structures, each distinct from each other with respect to their structures; one of ordinary skill in the art would not envision one in view of the other.

Claims 43-45 depend on claim 1, however, the claim comprises a method of administering a nucleic acid fragment, therefore, it has been placed in the groups comprising the methods of administering a nucleic acid (gene therapy), rather than the methods of administering a polypeptide and/or analogue.

6. (Groups 61-75 and 1-15/16-30), (Groups 76 and 1-15/16-30), and (Groups 77-91 and 31-60) are related as product and process of using. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)).

In the instant case the products of groups 61-76 can be used in a materially different process, such as Western blot, in addition to the methods of down-regulation recited.

In the instant case, the products of groups 77-91 can be used in a materially different process, such as hybridization, in addition to the methods of production and down-regulation recited.

7. Groups 77-94 and 1-60 are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)).

In the instant case, the products of Group 61-76 can be made by a materially different process, such as site-specific mutagenesis and PCR, in addition to the methods of peptide synthesis and genetic engineering recited.

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8. These inventions are distinct for the reasons given above. In addition, they have acquired a separate status in the art as shown by different classification and/or recognized divergent subject matter. Further, even though in some cases the classification is shared, a different field of search would be required based upon the structurally distinct products recited and the various methods of use comprising distinct method steps. Therefore restriction for examination purposes as indicated is proper.

Species Election

9. Applicant is further required under 35 USC 121 (1) to elect a single disclosed species to which the claims would be restricted if no generic claim is finally held to be allowable and (2) to list all claims readable thereon including those subsequently added.

(A) If Groups 1-30 are elected, applicant is required to elect a specific method for *in vivo* down-regulation of GDF-8 comprising administering a specific GDF-8 polypeptide and/or analogue (e.g. SEQ ID NO: 11; SEQ ID NO: 12 **OR** a GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (A) is introduced *linked* to a carrier molecule **OR** a GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (A) is introduced *without* a carrier molecule; or a polypeptide or analogue formulated with an adjuvant, etc.).

If applicant elects a method with a modified GDF-8, applicant is further required to elect a specific position to be modified as recited in claim 17 (e.g. residues 1-12).

Applicant is further required to elect a specific method wherein the immune system is effected by a specific number of copies of the GDF-8 polypeptide or analogue (claim 18).

If applicant elects a method with an adjuvant, applicant is further required to elect a specific adjuvant as recited in claim 22 (e.g. an adjuvant which facilitates breaking of autotolerance to autoantigens).

These species are distinct because the methods for *in vivo* down-regulation of GDF-8 differ with respect to the structure and mode of action of the specific polypeptide and/or analogue; thus each specific method employing a specific polypeptide and/or analogue represents patentably distinct subject matter. Currently, claim 1 is generic

Applicant is reminded to pick one ultimate species of these specific methods comprising ONE specific structure.

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(B) If Groups 31-60 are elected, applicant is required to elect a specific method for *in vivo* down-regulation of GDF-8 comprising administering a specific nucleic acid sequence encoding a specific GDF-8 polypeptide and/or analogue (e.g. SEQ ID NO: 11; SEQ ID NO: 12 **OR** a GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety **(A)** is introduced *linked* to a carrier molecule **OR** a GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety **(A)** is introduced *without* a carrier molecule; or a polypeptide or analogue formulated with an adjuvant).

Applicant is further required to elect a specific type of nucleic acid (e.g. naked DNA, DNA formulated with charged lipids, or DNA in a viral vector, etc.).

These species are distinct because the methods for *in vivo* down-regulation of GDF-8 comprising administering a specific nucleic acid sequence encoding a specific GDF-8 polypeptide and/or analogue differ with respect to structure of the nucleic acid sequences and compositions thereof; thus each specific method employing a specific nucleic acid sequence represents patentably distinct subject matter. Currently, claims 24 and 43 are generic.

Applicant is reminded to pick one ultimate species of these specific methods comprising ONE specific structure.

(C) If Groups 77-91 are elected, applicant is required to elect a specific nucleic acid comprising a specific vector (e.g. a plasmid or a phage or a cosmid, etc.) which is introduced into a specific host cell (e.g. a bacteria or a virus or a yeast or a protozoan, etc.) either integrated or not integrated into a host genome, with or without a carrier, vehicle, or adjuvant.

If applicant elects, a bacterium, virus, or insect cell, applicant is further required to elect a specific bacterium or a specific insect cell (e.g. the bacterium and insect cells recited in claim 41).

If applicant elects an adjuvant, applicant is further required to elect a specific adjuvant as recited in claim 22 (e.g. an adjuvant which facilitates breaking of autotolerance to autoantigens).

Applicant is reminded to pick one ultimate species of these specific nucleic acids, etc. comprising ONE specific structure.

These species are distinct because the nucleic acids, vectors, host cells, and compositions differ with respect to structure of the nucleic acid sequences and compositions thereof; thus each specific compound or composition comprising a specific nucleic acid sequence represents patentably distinct subject matter. Currently, claim 34 is generic.

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(D) If Groups 77-94 are elected, applicant is required to elect a specific method of either peptide synthesis or genetic engineering wherein a specific set of residues is to be mutated (e.g. residues 1-12) as recited in claim 17.

These species are distinct because each specific nucleic acid and amino acid sequence differs with respect to its structure and mode of action (e.g. introducing a Th epitope or effecting targeting to APC, etc.); thus each specific method comprising a specific mutated nucleic acid or amino acid sequence represents patentably distinct subject matter. Currently, claims 34, 43, and 50-51 are generic.

(E) If Groups 61-75 are elected, applicant is required to elect a specific GDF-8 analogue (e.g. SEQ ID NO: 11; or SEQ ID NO: 12; or a GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (A) is introduced *linked* to a carrier molecule; OR a GDF-8 analogue, wherein the analogue has been modified so that at least one foreign Th epitope moiety (A) is introduced *without* a carrier molecule; OR a polypeptide or analogue formulated with an adjuvant, etc.).

If applicant elects a modified GDF-8, applicant is further required to elect a specific position to be modified as recited in claim 17 (e.g. residues 1-12).

Applicant is further required to elect a specific analogue wherein the immune system is effected by a specific number of copies of the GDF-8 polypeptide or analogue (claim 18).

If applicant elects an analogue with an adjuvant, applicant is further required to elect a specific adjuvant as recited in claim 22 (e.g. an adjuvant which facilitates breaking of autotolerance to autoantigens).

These species are distinct because the GDF-8 analogues differ with respect to the structure and mode of action of the specific analogue; thus each specific analogue represents patentably distinct subject matter. Currently, claim 30 is generic

Applicant is reminded to pick one ultimate species of these specific analogues comprising ONE specific structure.

10. Applicant is advised that a response to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. § 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. M.P.E.P. § 809.02(a).

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Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. § 103 of the other invention.

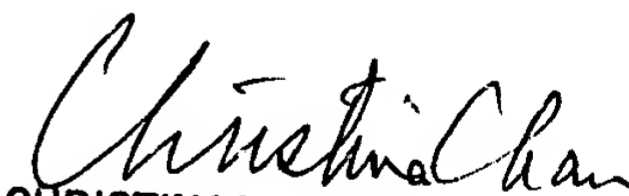
11. Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

12. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Megan Jamroz whose telephone number is (703) 308-8365. The examiner can normally be reached Monday through Friday from 8:00 AM to 4:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Margaret (Megan) Jamroz, Ph.D.
Patent Examiner
Technology Center 1600
February 25, 2002


CHRISTINA Y. CHAN
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GROUP 1800 1644